QUIZ NAVIGATION

Rose Wang

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Started on	Friday, 11 October 2024, 4:59 AM
State	Finished
Completed on	Friday, 11 October 2024, 5:04 AM
Time taken	5 mins 15 secs
Marks	5.0/10.0
Grade	**50.0** out of 100.0

Question 1

ID: 50135

Incorrect

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WD, a 71-year-old male, is admitted to the hospital due to an acute manic episode associated with his bipolar disorder. As the hospital pharmacist on the Acute Mental Health ward, you review his medication orders and see that he has been on lithium for many years. WD states that he has not been following up with his outpatient psychiatrist, so you want to ensure that his lithium is being appropriately monitored.

Which of the following is true regarding the appropriate monitoring of patients taking lithium for bipolar disorder?

Select one:

a. Higher lithium levels should be targeted during the maintenance phase when compared to acute mania ✖

b. Elderly patients require higher lithium target levels than the adult population due to pharmacodynamic changes ✖

c. Regular monitoring of hepatic function is recommended, as lithium is heavily metabolized by the liver ✖

Rose Wang (ID:113212) this answer is incorrect. Lithium is not heavily metabolized by the liver; it is largely excreted unchanged in the urine.

d. Regular calcium monitoring is recommended, as lithium can cause hypercalcemia ✔

Incorrect

Marks for this submission: 0.0/1.0.

TOPIC: Bipolar Disorder

LEARNING OBJECTIVE:

To learn about the appropriate monitoring of patients taking lithium.

BACKGROUND:

Lithium is a mood-stabilizing drug most often prescribed for bipolar disorder. The exact mechanism of action of lithium is currently unknown. Lithium can be used in all 3 phases of management for bipolar 1 disorder (acute mania, acute depression, maintenance therapy).

Lithium levels must be monitored to make sure the levels are not in the toxic range. Lithium levels for treating acute mania are 0.8-1.2 mmol/L. Lithium levels for maintenance therapy are 0.6-1 mmol/L. Elderly patients may require lower lithium targets (0.4-0.8 mmol/L for any phase), as they are more susceptible to lithium toxicity. The half-life of lithium in a healthy adult patient is 24 hours. In order to get an accurate level, the trough level must be taken 4-5 half-lives after the start of therapy/change in dose.

Lithium has many important drug and food interactions which can precipitate toxicities, such as changes in salt and water intake, ACE inhibitors, and diuretics.

Some adverse effects include weight gain, chronic tremors, hypothyroidism, hypercalcemia, cognitive impairment, and skin conditions such as acne and eczema. More serious safety concerns include QTc prolongation, T-wave changes, and renal toxicity, (including acute kidney injury, chronic kidney disease, and persistent polyuria).

In addition to serum lithium levels, relevant monitoring parameters include renal function, thyroid function, and serum calcium. Renal function monitoring is recommended, as lithium can cause renal toxicity, which can lead to the accumulation of lithium, and subsequently, further kidney damage. Thyroid status should be monitored, as lithium can cause hypothyroidism as an adverse effect. Similarly, lithium is associated with hypercalcemia, thus serum calcium monitoring is recommended.

RATIONALE:

Correct Answer:

- **Regular calcium monitoring is recommended, as lithium can cause hypercalcemia** - Hypercalcemia is a commonly reported side effect of lithium. As such, it is important to monitor a patient's calcium levels regularly.

Incorrect Answers:

- **Higher lithium levels should be targeted during the maintenance phase when compared to acute mania** - Lithium targets for acute mania (0.8-1.2 mmol/L) are higher than target levels for maintenance therapy (0.6-1 mmol/L).

- **Elderly patients require higher lithium target levels than the adult population due to pharmacodynamic changes** - In elderly patients, clinician should aim for lower target levels compared to the general adult population.
- **Regular monitoring of hepatic function is recommended, as lithium is heavily metabolized by the liver** - Lithium is not heavily metabolized by the liver; it is largely excreted unchanged in the urine.

TAKEAWAY/KEY POINTS:

Since lithium can cause hypercalcemia as an adverse effect, serum calcium levels should be monitored on a regular basis.

REFERENCE:

[1] Compendium of Pharmaceuticals and Specialties, Ottawa, ON: Canadian Pharmacists Association, https://myrxtx.ca.

The correct answer is: Regular calcium monitoring is recommended, as lithium can cause hypercalcemia

Question 2
ID: 48275
Correct
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HL is a 27-year-old female who works as a security guard at a teaching hospital in the city. She often has to deal with aggressive, angry patients. When she was a child, she was knocked down by a shoplifter running out of a store and suffered a concussion. This experience inspired her to choose security guarding a s a career. She works long hours and relies on microwave meals to keep her full. On her nights off, she likes to let loose by attending parties where she often tries 'little white pills.' Her family noticed that she was behaving differently and so they suggested she go see the doctor, who diagnosed her with bipolar disorder.

All of the following increase HL's risk of bipolar disorder **EXCEPT:**

Select one:

a. Head trauma ✖
b. Substance abuse ✖
c. Eating microwave meals ✔
d. Stress ✖

Rose Wang (ID:113212) this answer is correct. While proper nutrition is always important, it does not affect the risk of someone developing bipolar disorder.

Correct
Marks for this submission: 1.0/1.0.

TOPIC: Bipolar Disorder

LEARNING OBJECTIVE:

To learn about the risk factors associated with the development of bipolar disorder.

BACKGROUND:

Bipolar disorder affects approximately 2.4% of the world's population, and usually presents in adolescence or young adulthood, with an average age of onset of 25 years old. The exact causes of BD are unknown, however, it is thought that many factors including family history, neurotransmitter imbalance (including serotonin, norepinephrine, and dopamine), environmental and psychological stressors, poor sleep, stress, history of head trauma and perinatal insult can contribute to the disorder's pathogenesis. Central Nervous System (CNS) disorders (e.g. brain injury, stroke, or brain tumour), infections, and electrolyte/endocrine disorders (e.g. hyper/hypothyroidism, Cushing's disease, or hyper/hypoglycemia) may precipitate an episode of mania in all patients (including in those with BD). In addition, some medications and substances have been associated with BD and may precipitate a manic episode (including in situations of drug toxicity or withdrawal).

RATIONALE:

Correct Answer:

- **Proper nutrition does not affect the risk** - While proper nutrition is always important, it does not affect the risk of someone developing bipolar disorder.

Incorrect Answers:

- **Head trauma** - Head trauma increases the risk of someone developing bipolar disorder.
- **Substance abuse** - Substance abuse increases the risk of someone developing bipolar disorder.
- **Stress** - Stress increases the risk of someone developing bipolar disorder.

TAKEAWAY/KEY POINTS:

Head trauma, stress, substance abuse, family history, and perinatal insult all increase the risks of someone developing bipolar disorder.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. Bipolar Disord. 2021;23(8):767-788. doi:10.1111/bdi.13135
[2] Parikh SV. Bipolar Disorder. In: Compendium of Therapeutic Choices. Canadian Pharmacists Association.

The correct answer is: Eating microwave meals

Question 3
ID: 50137
Correct
Flag question
Send Feedback

DV, a 22-year-old female, arrives at the pharmacy accompanied by her mother. DV has a medical history that includes bipolar disorder type 1 and asthma. She has no known allergies. Her current medications include fluticasone 100 mcg 1 puff BID, salbutamol 100 mcg 2 puffs QID PRN for shortness of breath, as well as a combined oral contraceptive pill once daily. DV's mother informs you that DV has stopped taking her lithium due to intolerable side effects, which is why they are presenting with a new prescription for quetiapine. Both DV and her mother are worried that she may not tolerate the quetiapine and would like to know about the potential adverse effects of the medication.

Which of the following adverse effects is the most likely to with quetiapine?

Select one:

a. Insomnia ✖
b. Weight gain ✔
c. Extrapyramidal symptoms ✖
d. Hyperprolactinemia ✖

Rose Wang (ID:113212) this answer is correct. Quetiapine is associated with a high risk of weight gain.

Correct
Marks for this submission: 1.0/1.0.

TOPIC: Bipolar Disorders

LEARNING OBJECTIVE:

To learn the adverse effects associated with quetiapine therapy.

BACKGROUND:

Pharmacological treatments for each phase are determined by their level of evidence in treating the specified phase, as well as some other factors including but not limited to side effects, tolerability, drug interactions, and comorbid conditions. The mainstay treatments for bipolar disorder include lithium, valproic acid/divalproex, and Second Generation Antipsychotics (SGAs). Both monotherapy and combination therapy can be considered, however combination therapy is typically reserved for those with severe bipolar disorder. Combination therapy typically consists of a SGA and either lithium or divalproex. It is important to remember that those in manic or depressive states may have mixed features. In these cases, it is important to consider the recommended treatment options for the predominant episode. Second-generation antipsychotics are associated with lipid changes, blood glucose changes, weight gain, hyperprolactinemia, extrapyramidal symptoms (EPS), headaches, orthostatic hypotension, sedation or insomnia, QT prolongation, rare skin reactions, and GI side effects (e.g. constipation). Antipsychotics differ in their likelihood of causing each of these adverse effects. Of the second-generation antipsychotics used in the treatment of bipolar disorder, olanzapine and quetiapine are associated with the highest risk of weight gain. The risk of weight gain associated with risperidone, aripiprazole, lurasidone, and paliperidone is low to moderate. Asenapine and ziprasidone are associated with minimal or no weight gain. Hyperprolactinemia is most commonly associated with paliperidone and risperidone. Olanzapine and ziprasidone have a low risk of causing hyperprolactinemia. Aripiprazole, asenapine, lurasidone, and quetiapine carry a minimal risk of causing hyperprolactinemia. Aripiprazole and paliperidone carry a low risk of causing insomnia. The risk of insomnia is even lower with risperidone and ziprasidone. The risk is lowest (minimal to none) with asenapine, lurasidone, olanzapine, and quetiapine. Among the second-generation antipsychotics used to treat bipolar disorder, aripiprazole, paliperidone, and risperidone are associated with a low-to-moderate risk of extrapyramidal symptoms. Asenapine, lurasidone, and ziprasidone are associated with an even lower risk of extrapyramidal symptoms. Olanzapine and quetiapine carry a minimal risk of causing extrapyramidal symptoms.

RATIONALE:

Correct Answer:

- **Weight gain** - Quetiapine is associated with a high risk of weight gain.

Incorrect Answers:

- **Insomnia** - The risk of insomnia is minimal in patients taking quetiapine.
- **Extrapyramidal symptoms** - The risk of developing extrapyramidal symptoms is minimal in patients taking quetiapine.
- **Hyperprolactinemia** - Quetiapine is associated with a negligible risk of hyperprolactinemia.

TAKEAWAY/KEY POINTS:

Antipsychotics are associated with various adverse effects, including sleep disturbances (sedation or insomnia), extrapyramidal symptoms, weight gain, metabolic abnormalities, and hyperprolactinemia. Quetiapine is associated with a higher risk of sedation, weight gain, and metabolic abnormalities. It is associated with a minimal risk of causing insomnia, extrapyramidal symptoms, and hyperprolactinemia.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. Bipolar Disord. 2021;23(8):767-788. doi:10.1111/bdi.13135

bipolar disorder with mixed presentations. Bipolar Disord. 2021;23(8):767-788. doi:10.1111/bdi.13155
[2] Milliken H. Psychoses. In: Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca
[3] Quetiapine Product Monograph; https://pdf.hres.ca/dpd_pm/00063750.PDF

The correct answer is: Weight gain

Question 4
ID: 42192
Incorrect
Flag question
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You are working as the Clinical Pharmacist on a Family Health Team. One of the primary care physicians asks for your treatment recommendation on a case of hers. Her patient is a 26-year-old male with a new diagnosis of bipolar type 1 disorder. He is currently experiencing an acute manic episode. He is very hesitant to start any medications, so the physician is concerned about medication compliance. She would like to try to utilize the same medication for his initial mania therapy as well as for his maintenance therapy, to hopefully improve compliance by maintaining medication consistency.

Which agent is considered first-line monotherapy for both acute mania and maintenance therapy in bipolar disorder?

Select one:

a. Lamotrigine ✖
b. Lurasidone ✖
c. Risperidone ✖

Rose Wang (ID:113212) this answer is incorrect. Risperidone is a first-line option for manic episodes, but it is not considered a first-line agent for maintenance therapy in patients with bipolar disorder.

d. Asenapine ✔

Incorrect
Marks for this submission: 0.0/1.0.

TOPIC: Bipolar Disorder

LEARNING OBJECTIVE:

To identify which agents are first-line options in the treatment of the different phases of bipolar disorder.

BACKGROUND:

Pharmacological treatments for each phase are determined by their level of evidence in treating the specified phase, as well as some other factors including but not limited to side effects, tolerability, drug interactions, and comorbid conditions. The mainstay treatments for bipolar disorder include lithium, valproic acid/divalproex, and Second-Generation Antipsychotics (SGAs). Combination therapy typically consists of a SGA and either lithium or divalproex. It is important to remember that those in manic or depressive states may have mixed features. In these cases, it is important to consider the recommended treatment options for the predominant episode.

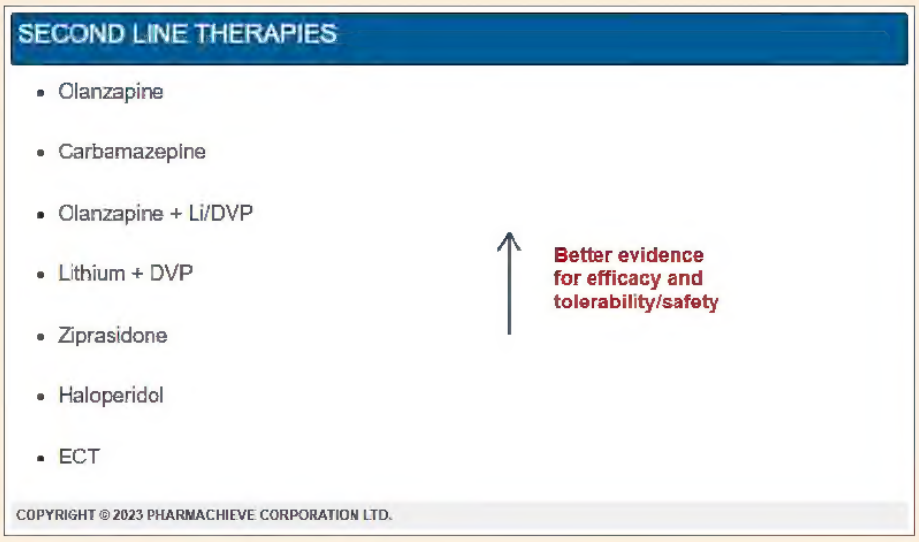
Manic Episodes

Both monotherapy and combination therapy are first-line options for acute mania, depending on the patient. About 50% of patients respond to monotherapy and about 70% respond to combination therapy. However combination therapy is associated with more side effects compared to monotherapy. As a result, combination therapy is generally reserved for patients who require a quicker response, have more severe symptoms, have had a partial or no response to monotherapy, and who will likely tolerate combination therapy (based on their previous response to BD treatments, and age).

Improvement in mania usually occurs within 1-2 weeks. If a therapeutic response is not seen after 2 weeks, assess patients for external factors such as adherence and possible substance use and optimize dosing if possible. If drug therapy has already been optimized, a switch to a different first-line agent is warranted (especially if there was no response to the initial agent). If the disease is particularly severe, if the initial agent was well-tolerated and provided some benefit, add-on of a second agent can also be considered. An additional 2 weeks should be given to monitor the effects of these changes. Second- and third-line therapies should only be trialled if all previous options have been tried or ruled out. If a therapeutic improvement is seen, continue on the current regimen for at least 2 months, until the patient enters the maintenance phase. The 2018 CANMAT treatment recommendations for acute mania in bipolar disorder are outlined below:

FIRST LINE MONOTHERAPIES		FIRST LINE COMBINATION THERAPIES	
• Lithium • Quetiapine • Divalproex/Valproic Acid • Asenapine • Aripiprazole • Paliperidone >6mg • Risperidone	↑ Better evidence for efficacy and tolerability/safety	• Quetiapine + Li/DVP • Aripiprazole + Li/DVP • Risperidone + Li/DVP • Asenapine + Li/DVP	↑ Better evidence for efficacy and tolerability/safety

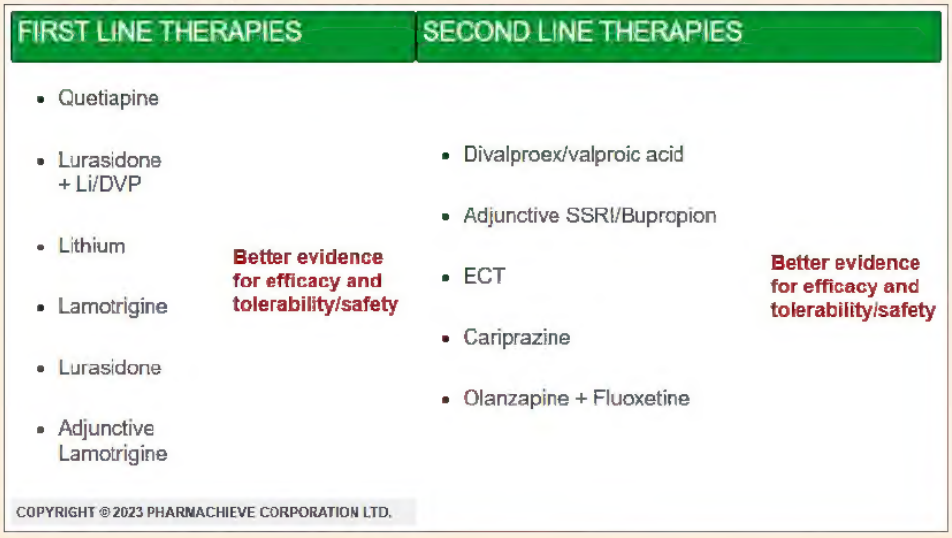
- Risperidone
- Cariprazine



Depressive Episodes

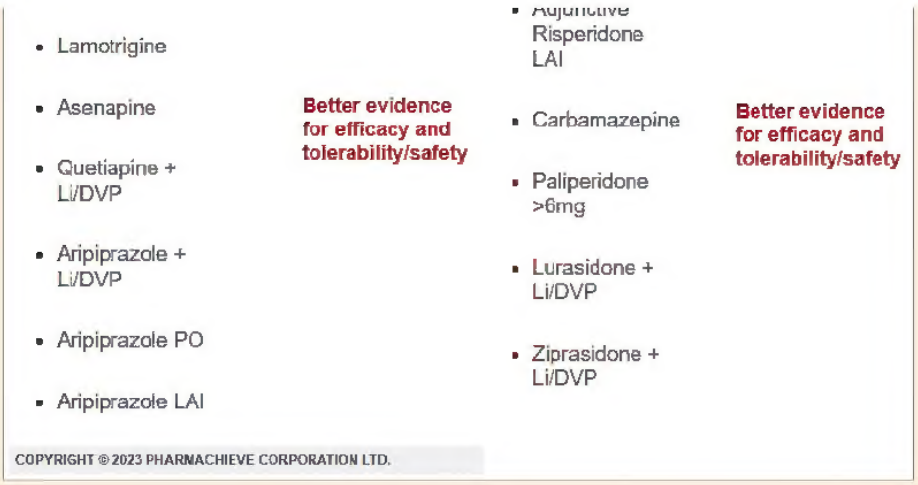
Similar to treating manic episodes, most first-line and second-line regimens have comparable efficacy in treating acute bipolar depression. Thus, evidence in the maintenance phase, in treating acute manic episodes, as well as safety and tolerability are used to determine treatment hierarchy.

Although difficult to treat, drug response in bipolar depression is expected within 2-4 weeks. If a response is not seen after this time, consider assessing patients for external factors such as adherence and possible substance use and optimizing drug therapy. If these have already been optimized, a switch to a different first-line agent or adding a new agent is warranted. An additional 2-4 weeks should be given to monitor the response to these changes. Second- and third-line therapies should only be trialled if all previous options have been tried or ruled out. If therapeutic improvement is seen, continue on the current regimen for at least 2 months, until the patient enters the maintenance phase. The 2018 CANMAT treatment recommendations for acute depression in bipolar disorder are outlined below:



Maintenance Therapy

As stated previously, patients are considered to be in maintenance after experiencing minimal to no symptoms on therapy for at least 2 months. Without therapy, 23-40% of patients will experience a recurrent BD episode within 1 year. Maintenance therapy reduces this to 19-25%, reduces residual symptoms following acute episodes, and restores daily functioning. Maintenance therapy for BD is generally lifelong. The 2018 CANMAT treatment recommendations for maintenance therapy are outlined below:



RATIONALE:

Correct Answer:

(Choice #4): Asenapine is a first-line option for manic episodes and maintenance therapy in patients with bipolar disorder.

Incorrect Answers:

(Choice #1): Lamotrigine is considered a first-line option for depressive episodes and maintenance therapy in patients with bipolar disorder. It is not recommended as first-line therapy for patients with acute manic episodes.

(Choice #2): Lurasidone is not considered a first-line option for manic episodes or maintenance therapy in patients with bipolar disorder.

(Choice #3): Risperidone is a first-line option for manic episodes, but it is not considered a first-line agent for maintenance therapy in patients with bipolar disorder.

TAKEAWAY/KEY POINTS:

Existing evidence surrounding various pharmacologic agents guides their roles in therapy for each phase of bipolar disorder. Asenapine is considered a first-line agent for acute manic episodes and maintenance therapy in patients with bipolar disorder.

REFERENCES:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord*. 2021;23(8):767-788. doi:10.1111/bdi.13135

[2] Parikh SV. Bipolar Disorder. In: Compendium of Therapeutic Choices. Canadian Pharmacists Association.

The correct answer is: Asenapine

Question 5

ID: 50138

Incorrect

Flag question

Send Feedback

EB is a 56-year-old male presenting to the hospital accompanied by his wife. According to his wife, EB has been getting minimal sleep over the past few days, and has been rambling about building "the next big empire of cleaning supplies". EB is diagnosed as having an acute manic episode. In addition to his presenting symptoms, EB has a history of hypertension, hypothyroidism, and type 2 diabetes. His current medication regimen includes ramipril 10 mg once daily, hydrochlorothiazide 25 mg once daily, levothyroxine 88 mcg once daily, metformin 1000 mg twice daily, and sitagliptin 100 mg once daily.

Which of the following agents is the most likely to be contributing to EB's symptoms of mania?

Select one:

a. Hydrochlorothiazide ✖

Rose Wang (ID:113212) this answer is incorrect. It is unlikely that the patient's hydrochlorothiazide contributed significantly to his symptoms.

b. Sitagliptin ✖

c. Levothyroxine ✔

d. Ramipril ✖

Incorrect

Marks for this submission: 0.0/1.0.

TOPIC: Bipolar Disorders

LEARNING OBJECTIVE:

To identify drugs that may precipitate mania.

BACKGROUND:

Bipolar disorder affects approximately 2.4% of the world's population, and usually presents in adolescence or young adulthood, with an average age of onset of 25 years old. The exact causes of BD are unknown, however, it is thought that many factors including family history, neurotransmitter imbalance (including serotonin, norepinephrine, and dopamine), environmental and psychological stressors, and poor sleep can contribute to the disorder's pathogenesis. Central Nervous System (CNS) disorders (e.g. brain injury, stroke, or brain tumour), infections, and electrolyte/endocrine disorders (e.g. hyper/hypothyroidism, Cushing's disease, or hyper/hypoglycemia) may precipitate an episode of mania in all patients (including in those with BD). In addition, some medications and substances have been associated with BD and may precipitate a manic episode (including in situations of drug toxicity or withdrawal)

Agents that may precipitate mania:

- Alcohol
- Antidepressants, such as Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), bupropion, and Monoamine Oxidase Inhibitors (MAOIs)
- Caffeine
- Decongestants (e.g., pseudoephedrine and phenylephrine)
- Parkinsonian/dopamine augmenting drugs: levodopa (prodrug of dopamine), dopamine agonists (e.g., ropinirole, bromocriptine, and pramipexole), dopamine reuptake inhibitors (e.g., amantadine and benztropine)
- Hallucinogens, such as lysergic acid diethylamide (LSD) and phenylcyclohexyl piperidine (PCP)
- Herbals (e.g., St. John's Wort, ephedra, and ginseng)
- Marijuana
- Norepinephrine augmenting agents: alpha-2-agonists (e.g. clonidine, guanfacine, and tizanidine), beta agonists (e.g. epinephrine, norepinephrine, and dobutamine)
- Steroids
- Stimulants (e.g, amphetamine and cocaine)
- Thyroid preparations
- Withdrawal of: alcohol, alpha-2-agonists, antidepressants, barbiturates, benzodiazepines, opiates

RATIONALE:

Correct Answer:

- **Thyroid preparations** - Thyroid preparations like levothyroxine can precipitate mania.

Incorrect Answers:

- **Hydrochlorothiazide** - It is unlikely that the patient's hydrochlorothiazide contributed significantly to his symptoms.
- **Sitagliptin** - It is unlikely that the patient's sitagliptin contributed significantly to his symptoms.
- **Ramipril** - It is unlikely that the patient's ramipril contributed significantly to his symptoms.

TAKEAWAY/KEY POINTS:

There are various drugs and drug classes that can precipitate mania. These include alcohol, antidepressants, caffeine, decongestants, dopamine augmenting drugs, hallucinogens, herbal products, marijuana, norepinephrine augmenting agents, steroids, stimulants, and thyroid preparations. Additionally withdrawal from alpha-2-agonists, antidepressants, barbiturates, benzodiazepines, and opiates may contribute to manic symptoms.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord.* 2021;23(8):767-788. doi:10.1111/bdi.13135.
[2] Haygood J, Drayton SJ. Bipolar Disorder. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM, eds. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023. accesspharmacy.mhmedical.com/content.aspx?aid=1206641688

The correct answer is: Levothyroxine

Question 6

ID: 50141

Incorrect

Flag question

Send Feedback

KR is a 45-year-old male presenting to the doctor's office accompanied by his wife. According to his wife, KR has been speaking much faster than normal and she cannot understand him. When she asks him to slow down and re-explain things to her, he gets frustrated and annoyed which scares her. When she asked him to help make dinner, he left the stove on halfway through and found him practicing the guitar for what he describes as his 'next hit single.' KR is usually a reserved, quiet and gentle person so his wife is understandably concerned. KR is diagnosed as having an acute manic episode.

Given the severity of KRs symptoms, the physician would like to initiate combination therapy. Which of the following medication combinations is considered first-line therapy for acute mania in bipolar disorder?

Select one:

a. Lithium + Divalproex ✖

b. Lurasidone + Lithium ✖

Rose Wang (ID:113212) this answer is incorrect. The combination of lurasidone and lithium is not a recommended therapy for bipolar mania.

c. Ziprasidone + Divalproex ✖

d. Risperidone + Lithium ✔

Incorrect

Marks for this submission: 0.0/1.0.

TOPIC: Bipolar Disorder

LEARNING OBJECTIVE:

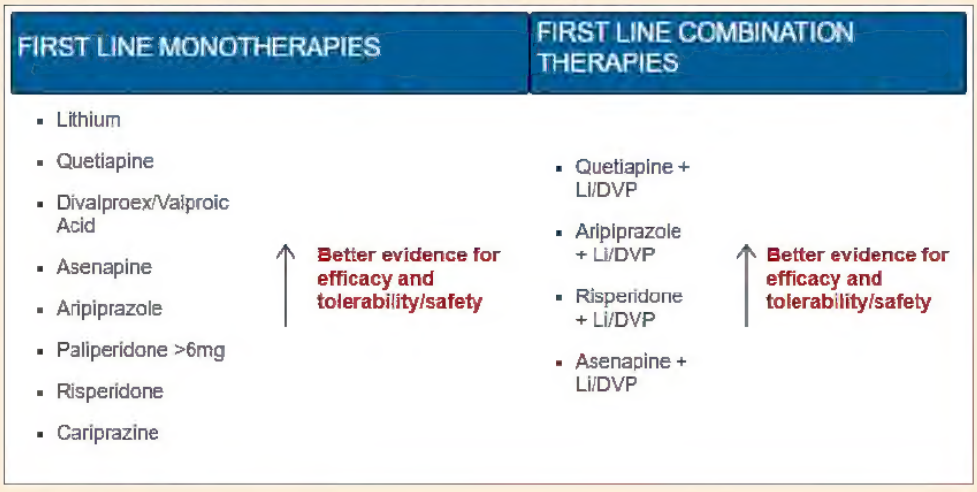
To identify first-line drug combinations for the treatment of acute mania in patients with bipolar disorder.

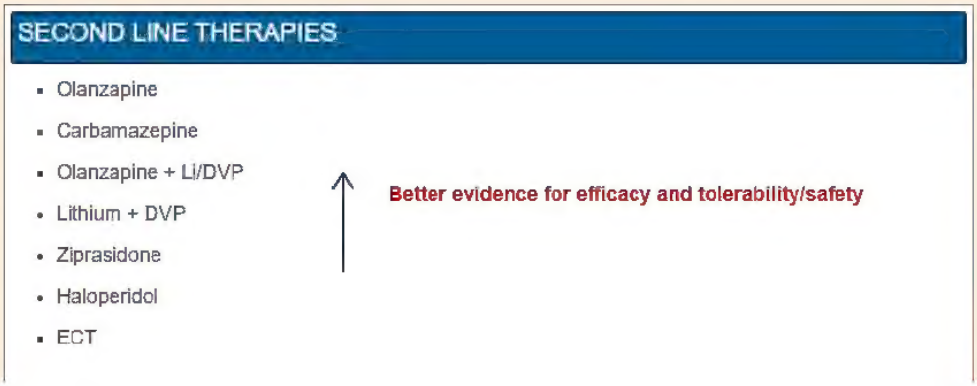
BACKGROUND:

Pharmacological treatments for each phase are determined by their level of evidence in treating the specified phase, as well as some other factors including but not limited to side effects, tolerability, drug interactions, and comorbid conditions. The mainstay treatments for bipolar disorder include lithium, valproic acid/divalproex, and Second-Generation Antipsychotics (SGAs). Combination therapy typically consists of a SGA and either lithium or divalproex. It is important to remember that those in manic or depressive states may have mixed features. In these cases, it is important to consider the recommended treatment options for the predominant episode.

Manic Episodes

Both monotherapy and combination therapy are first-line options for acute mania, depending on the patient. About 50% of patients respond to monotherapy and about 70% respond to combination therapy. However, combination therapy is associated with more side effects compared to monotherapy. As a result, combination therapy is generally reserved for patients who require a quicker response, have more severe symptoms, have had a partial or no response to monotherapy, and who will likely tolerate combination therapy (based on their previous response to BD treatments, and age). Improvement in mania usually occurs within 1-2 weeks. If a therapeutic response is not seen after 2 weeks, assess patients for external factors such as adherence and possible substance use and optimize dosing if possible. If drug therapy has already been optimized, a switch to a different first-line agent is warranted (especially if there was no response to the initial agent). If the disease is particularly severe, if the initial agent was well-tolerated and provided some benefit, add-on of a second agent can also be considered. An additional 2 weeks should be given to monitor the effects of these changes. Second- and third-line therapies should only be trialled if all previous options have been tried or ruled out. If a therapeutic improvement is seen, continue on the current regimen for at least 2 months, until the patient enters the maintenance phase. The 2018 CANMAT treatment recommendations for acute mania in bipolar disorder are outlined below:





RATIONALE:

Correct Answer:

- **Risperidone + lithium** - The combination of risperidone and lithium is considered a first-line therapy for the treatment of bipolar mania.

Incorrect Answers:

- **Lithium + divalproex** - The combination of lithium and divalproex is considered a second-line therapy for the treatment of bipolar mania.
- **Lurasidone + lithium** - The combination of lurasidone and lithium is not a recommended therapy for bipolar mania.
- **Ziprasidone + divalproex** - The combination of ziprasidone and divalproex is not a recommended therapy for bipolar mania.

TAKEAWAY/KEY POINTS:

Quetiapine, aripiprazole, risperidone, or asenapine may be combined with either lithium or divalproex to form a first-line combination therapy for the treatment of bipolar mania.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord.* 2021;23(8):767-788. doi:10.1111/bdi.13135.

The correct answer is: Risperidone + Lithium

Question 7

ID: 50143

Correct

Flag question

Send Feedback

PR, a 35-year-old entrepreneur, has recently caught the attention of his colleagues due to his unusually energetic and impulsive behaviour. Friends have noticed that he has been talking rapidly, sleeping less, and taking on multiple projects simultaneously. Concerns about his well-being led him to seek medical attention. After a thorough evaluation, PR is diagnosed with bipolar disorder, specifically bipolar type 1, during an ongoing acute manic episode. PR has no known allergies but his past medical history is significant for dyslipidemia. He currently takes atorvastatin 40 mg PO QHS. Prior to this episode, PR was quite active as he enjoys cycling 3 days per week. PR's psychiatrist decides to initiate lithium for his acute manic episode.

All of the following statements are correct regarding lithium therapy for bipolar disorder **EXCEPT**:

Select one:

a. Lithium should be intermittently held in acute illnesses where fluid and electrolyte depletion are present ✖

b. Lithium can more commonly cause hyperthyroidism as compared to hypothyroidism ✔

Rose Wang (ID:113212) this answer is correct. Lithium can cause hypothyroidism as a side effect. In very rare cases, hyperthyroidism has been observed, however, hypothyroidism is much more common.

c. Renal function should be monitored at least twice yearly ✖

d. Ataxia is a sign of lithium toxicity ✖

Correct

Marks for this submission: 1.0/1.0.

TOPIC: Bipolar Disorders

LEARNING OBJECTIVE:

Identify treatment-related practices which should be followed for patients on lithium therapy.

BACKGROUND:

Lithium is a mood-stabilizing drug most often prescribed for bipolar disorder. The exact mechanism of action of lithium is currently unknown. Lithium can be used in all 3 phases of management for bipolar 1 disorder (acute mania, acute depression, maintenance therapy).

Lithium has many important drug and food interactions which can precipitate toxicities, such as changes in salt and water intake, ACE inhibitors, NSAIDs, and diuretics.

NSAIDs, ACE inhibitors and diuretics can increase lithium levels by reducing its clearance from the kidneys. This, in turn, can lead to lithium toxicity (early symptoms can include muscle weakness and fatigue.)

Other measures to be monitored when on lithium therapy include renal function (monitor at least twice yearly).

Lithium should be intermittently held in acute illnesses where fluid and electrolyte depletion are present such as food poisoning or severe vomiting or diarrhoea. Changes in electrolytes and fluids can impact the clearance of lithium.

Side effects of lithium include diabetes insipidus, cardiac arrhythmias, hypothyroidism (rarely hyperthyroidism

can be seen), nausea, vertigo, muscle weakness (not an exhaustive list). These side effects should be counselled on and monitored for in all patients on lithium therapy.

Signs of lithium toxicity include ataxia, sedation, agitation, tremors, diarrhea, and vomiting.

RATIONALE:

Correct Answer:

- **Lithium can more commonly cause hyperthyroidism as compared to hypothyroidism** - In very rare cases, hyperthyroidism has been observed, however, hypothyroidism is much more common.

Incorrect Answers:

- **Lithium should be intermittently held in acute illnesses where fluid and electrolyte depletion are present** - Diarrhea, vomiting, decreased fluid intake, salt fluctuations can cause lithium toxicity due to hyponatremia. This statement is true but does not directly address the question of common side effects.
- **Renal function should be monitored at least twice yearly** - Lithium is renally cleared therefore renal function should be monitored to minimize the risk of side effects. This is a correct practice but the question specifically asked about side effects, not monitoring practices.
- **Ataxia is a sign of lithium toxicity** - Signs of lithium toxicity include ataxia, sedation, agitation, tremors, diarrhea, and vomiting. This statement is true but does not address the specific side effect discussed in the question stem.

TAKEAWAY/KEY POINTS:

Hypothyroidism as a complication of lithium therapy is more common than hyperthyroidism as a complication of lithium therapy.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord*. 2021;23(8):767-788. doi: 10.1111/bdi.13135
[2] Parikh SV. Bipolar Disorder. In: Compendium of Pharmaceuticals and Specialties. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca

The correct answer is: Lithium can more commonly cause hyperthyroidism as compared to hypothyroidism

Question 8
ID: 50145
Correct
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Which of the following interactions is expected to result from the co-administration of quetiapine and a CYP3A4 inhibitor like itraconazole?

Select one:

a. Increased risk of weight gain and sedation from quetiapine ✔

Rose Wang (ID:113212) this answer is correct. A CYP3A4 inhibitor like itraconazole is expected to increase serum levels of a CYP3A4 substrate like quetiapine, resulting in increased quetiapine toxicity (e.g. weight gain, sedation).

b. Decreased therapeutic activity of quetiapine ✖
c. Increased risk of nausea and diarrhea from itraconazole ✖
d. Decreased antifungal activity of itraconazole ✖

Correct
Marks for this submission: 1.0/1.0.

TOPIC: Bipolar Disorders

LEARNING OBJECTIVE:

To review relevant drug-drug interactions involving quetiapine.

BACKGROUND:

The cytochrome P450 enzymes are responsible for the metabolism of various drugs. Upon metabolism, a drug may be activated (e.g. metabolism of a prodrug into an active substance), converted into a metabolite with some physiological activity (often less than the parent compound), or converted into a metabolite with no physiological activity. An inducer of the cytochrome P450 pathway increases the activity of cytochrome P450 enzymes, whereas an inhibitor would inhibit the activity of these enzymes.

Quetiapine is metabolized by the CYP3A4 isozyme. A CYP3A4 inhibitor like itraconazole would slow the metabolism of quetiapine, thereby increasing serum quetiapine levels. As a result, increased adverse effects from quetiapine (e.g. weight gain, sedation) are to be expected.

RATIONALE:

Correct Answer:

- **Increased risk of weight gain and sedation from quetiapine** - A CYP3A4 inhibitor like itraconazole is expected to increase serum levels of a CYP3A4 substrate like quetiapine, resulting in increased quetiapine toxicity (e.g. weight gain, sedation).

Incorrect Answers:

- **Decreased therapeutic activity of quetiapine** - A CYP3A4 inhibitor like itraconazole is expected to increase serum levels of quetiapine. As such, a decrease in quetiapine's therapeutic activity is not expected to occur.
- **Increased risk of nausea and diarrhea from itraconazole OR Decreased antifungal activity of itraconazole** - Administration of a CYP3A4 substrate like quetiapine is not expected to affect the metabolism of a CYP3A4 inhibitor like itraconazole.

TAKEAWAY/KEY POINTS:

Quetiapine is metabolized by CYP3A4 and as such would have increased serum levels when given with CYP3A4 inhibitors like itraconazole.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord*. 2021;23(8):767-788. doi:10.1111/bdi.13135.
[2] Quetiapine Product Monograph; https://pdf.hres.ca/dpd_pm/00063750.PDF
[3] Parikh SV. Bipolar Disorder. In: Compendium of Pharmaceuticals and Specialties. Ottawa, ON: Canadian Pharmacists Association. https://myrxtx.ca.

The correct answer is: Increased risk of weight gain and sedation from quetiapine

Question 9

ID: 50151

Correct

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A 27-year-old male is started on valproic acid 500 mg PO BID for acute bipolar mania. Two months later, he is found to have depressive symptoms and lamotrigine is started.

The management of lamotrigine in the setting of valproic acid include:

Select one:

- Lamotrigine can be started at the regular dosing schedule and titrated over weeks ✖
- Lamotrigine plasma levels can increase up to 2 times with the concurrent use of valproic acid ✔

Rose Wang (ID:113212) this answer is correct. Valproic acid reduces the plasma clearance of lamotrigine, therefore lamotrigine needs to be initiated at a much lower dose (~50% reduced dose).

- Lamotrigine is an absolute contraindication in patients on valproic acid ✖
- Lamotrigine plasma levels can be up to 2 times lower on concurrent valproic acid therapy ✖

Correct

Marks for this submission: 1.0/1.0.

TOPIC: Bipolar disorder

LEARNING OBJECTIVE:

Understand the drug interaction between lamotrigine and valproic acid and its clinical implications.

BACKGROUND:

Lamotrigine is an antiepileptic drug that is effective in many different conditions apart from epilepsy. For example, lamotrigine is effective for depressive symptoms associated with bipolar 1 disorder. It is postulated that lamotrigine works by stabilizing neuronal membranes and inhibiting the release of neurotransmitters such as glutamate by acting on voltage-gated sodium channels.

Side effects of lamotrigine include rare drug rashes (e.g. Steven Johnson Syndrome), dizziness, headaches, nausea, sleepiness & ataxia to name a few.

Drug interactions mainly include drugs that affect glucuronidation, as lamotrigine is metabolized by glucuronidation. One major drug interaction clinicians need to be aware of is with valproic acid/divalproex. Valproic acid is a strong inhibitor of glucuronidation, and therefore when used concurrently with lamotrigine, lamotrigine levels can double in the plasma and lead to side effects. Their concurrent use is not contraindicated, but dose adjustments need to be made.

Lamotrigine should be started at a 50% reduced dose of the regular dose in patients taking valproic acid. The usual dose of lamotrigine is 50mg daily. It should be dropped to 25mg daily in patients on both drugs. There is also an even more conservative approach which recommends starting at 25mg every other day.

RATIONALE:

Correct Answer:

- **Lamotrigine plasma levels can increase up to 2 times with the concurrent use of valproic acid** - Valproic acid reduces the plasma clearance of lamotrigine, therefore, lamotrigine needs to be initiated at a much lower dose (~50% reduced dose).

Incorrect Answers:

- **Lamotrigine can be started at the regular dosing schedule and titrated over weeks** - Lamotrigine interacts with valproic acid.
- **Lamotrigine is an absolute contraindication in patients on valproic acid** - Lamotrigine is an absolute contraindication in patients on valproic acid. Lamotrigine interacts with valproic acid, but it is

not an absolute contraindication. While true, it does not fully address the need for dose adjustment.

- **Lamotrigine plasma levels can be up to 2 times lower on concurrent valproic acid therapy** - Valproic acid does NOT increase lamotrigine metabolism. This statement is incorrect; valproic acid does affect lamotrigine metabolism by reducing its clearance.

TAKEAWAY/KEY POINTS:

When initiating patients on lamotrigine who are already taking valproic acid, lamotrigine needs to be started at a lower dose than usual (often 50% reduction).

REFERENCE:

[1] Kanner AM. When Thinking of Lamotrigine and Valproic Acid, Think "Pharmacokinetically"! *Epilepsy Curr.* 2004;4(5):206-207. doi:10.1111/j.1535-7597.2004.04515.x. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1176375.

The correct answer is: Lamotrigine plasma levels can increase up to 2 times with the concurrent use of valproic acid

Question 10

ID: 43179

Incorrect

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All of the following drugs can be used first-line as maintenance therapy for Bipolar Disorder 1 **EXCEPT**:

Select one:

- Quetiapine ✖
- Divalproex ✖
- Asenapine ✖

Rose Wang (ID:113212) this answer is incorrect. Asenapine can be used as first line option.

- Carbamazepine ✔

Incorrect

Marks for this submission: 0.0/1.0.

TOPIC: Bipolar Disorder

LEARNING OBJECTIVE:

To identify first-line options for maintenance therapy of bipolar 1 disorder.

BACKGROUND:

Bipolar 1 disorder is a mood disorder that is characterized by changes in mood, energy, and behaviour. Patients must present with at least 1 episode of mania (symptoms include elevated mood, fast speech, feelings of grandiosity etc), with or without episodes of major depression. In bipolar 1 disorder management, there are 3 distinct phases that clinicians need to treat: acute mania, acute depression, and maintenance (e.g. prevention of recurrence). Drugs used for one of these phases may not necessarily be used for another of these phases. For example, a drug that is first-line for acute depression may not have any benefit in acute mania or maintenance therapy.

Below are the updated 2018 CANMAT recommendations for the maintenance therapy:

FIRST LINE THERAPIES	SECOND LINE THERAPIES
• Lithium • Quetiapine • Divalproex/Valproic Acid • Lamotrigine • Asenapine • Quetiapine + Li/DVP • Aripiprazole + Li/DVP • Aripiprazole PO • Aripiprazole OM	• Olanzapine • Risperidone LAI • Adjunctive Risperidone LAI • Carbamazepine • Paliperidone > 6mg • Lurasidone + Li/DVP • Ziprasidone + Li/DVP

Better evidence for efficacy and tolerability/safety (↑ first line)

Better evidence for efficacy and tolerability & safety (↑ second line)

RATIONALE:

Correct Answer:

(Option #4): Carbamazepine is second-line compared to all the other agents listed.

Incorrect Answers:

(Option #1): Quetiapine can be used as a first-line option.
(Option #2): Divalproex can be used as a first-line option.
(Option #3): Asenapine can be used as first-line option.

TAKEAWAY/KEY POINTS:

Carbamazepine is not a first-line option for the maintenance of bipolar 1 disorder. First-line therapies include lamotrigine, asenapine, and divalproex. Carbamazepine is a second-line agent.

REFERENCE:

[1] Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord.* 2021;23(8):767-788. doi:10.1111/bdi.13135.

The correct answer is: Carbamazepine

Finish review